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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,817	11/06/2000	Horst Loerz	514413-3849	5231

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	14

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,817	LOERZ ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-53* is/are pending in the application.

4a) Of the above claim(s) *30,33,34 and 51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-29,31,32 and 35-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 24-53 are pending.

Claims 47-53 have been added.

Claims 24-46 have been amended.

2. Applicant's election with traverse of Group I, claims 24-29, 31-32 and 35-46 including SEQ ID NO:1 encoding SEQ ID NO:2 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that the vector of claim 33 of Group III is almost identical to the vector of claim 31 of Group I and should be searched and examined together. This is not found persuasive because the vector of claim 33 also includes a nucleic acid molecule all of which are used as a mechanism to co-suppress a desired protein activity. While searches are over-lapping and co-extensive, search evaluations are still divergent.

Newly submitted claims 51-53 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 51 and 52 are directed to a protein and claim 53 is directed to a starch, all of which are inventions not originally presented in the initial set of claims.

The requirement is still deemed proper and is therefore made FINAL.

Claims 30, 33-34, and 51-53 are withdrawn from consideration because they are drawn to non-elected material.

Claims 24-29, 31-32, and 35-50, will be examined on their merits.

Specification

The abstract of the disclosure is objected to because it is more that one paragrah. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 24, 27, 32, 42, 45, and 47-48 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 and 47 are indefinite in the recitation "shown under". Amending the claim to recite --of-- will obviate the rejection.

Claim 27 is indefinite in the recitation "containing". Amending the claim to recite --comprising-- will obviate the rejection.

In claim 32, add the word --operably-- before the word "linked".

Claim 32 is indefinite in the recitation "pro-". Amending the claim to recite --prokaryotic-- will obviate the rejection.

Claim 42 is indefinite in the recitation "a starch-storing plant". All plants store starch to some degree in chloroplasts during photosynthesis. Are Applicants claiming all plants? Applicants have not set the metes and bounds of "starch-storing", as it relates to the plants Applicants are claiming.

Claim 45 is indefinite in the recitation "a propagation material". Applicant has not defined this term to explicitly state the metes and bounds of plant material that is encompassed in said recitation.

Claim 48 is indefinite in the recitation "at least about". It is not clear from Applicant's wording what the intention of the recitation is. Is Applicant claiming at least 65% or is Applicant claiming about 65% which can be interpreted in many different ways?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 24-29, 31-32, 35-50, and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Applicant claims an isolated nucleic acid molecule encoding a protein with the function of a wheat isoamylase selected from the group consisting of: a nucleic acid molecule encoding a protein of SEQ ID NO:2, a nucleic acid molecule of SEQ ID NO:1 or part thereof, a nucleic acid molecule which hybridizes to any of the before-mentioned sequences, and a degenerate nucleic acid of one of the before-mentioned sequences. Applicants also claim a nucleic acid molecule that hybridizes with a before-mentioned sequence and exhibits 65% or 90% homology to SEQ ID NO:1.

Applicants isolated their invention by screening a cDNA library constructed from wheat 21-day ("starchy" endosperm) old caryopses (page 30, last sentence) with a probe generated by amplifying the "sugary" isoamylase from maize. The clone Tasu-19 was isolated and sequenced and is shown as SEQ ID NO:1 whose encoded polypeptide exhibits homology to isoamylases and is shown as SEQ ID NO:2.

The Applicants do not identify structural features unique to the putative wheat isoamylase enzyme, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the wheat isoamylase protein, it remains unclear what features identify a wheat isoamylase protein, including a wheat isoamylase gene that hybridizes with SEQ ID NO:1 or part thereof or a sequence that exhibits 65% or 90% sequence homology with SEQ ID NO:1. Since a wheat isoamylase protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

5. Claims 24-29, 31-32, 35-50, and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Applicant claims an isolated nucleic acid molecule encoding a protein with the function of a wheat isoamylase selected from the group consisting of: a nucleic acid molecule encoding a protein of SEQ ID NO:2, a nucleic acid molecule of SEQ ID NO:1 or part thereof , a nucleic acid molecule which hybridizes to any of the before-mentioned sequences, and a degenerate nucleic acid of one of the before-mentioned sequences. Applicants also claim a nucleic acid molecule that hybridizes with a before-mentioned sequence and exhibits 65% or 90% homology to SEQ ID NO:1, including a host cell, process for preparing a protein, transgenic plant cell and plant, all of which comprise a before-mentioned sequence operably linked to regulatory elements which ensure transcription, wherein the plant is a monocot or maize plant. Lastly, Applicants claim a starch obtained from the host cell, plant cell, plant, and plant propagation material.

Applicants isolated their invention by screening a cDNA library constructed from wheat 21-day ("starchy" endosperm) old caryopses (page 30, last sentence) with a probe generated by amplifying the "sugary" isoamylase from maize. The clone Tasu-19 was isolated and sequenced and is shown as SEQ ID NO:1 whose encoded polypeptide exhibits homology to isoamylases and is shown as SEQ ID NO:2.

It cannot be predicted by one of skill in the art that nucleic acids that have 65% or 90% homology to SEQ ID NO:1 or that hybridize to SEQ ID NO:1 or fragments thereof will encode a protein with the same activity as the wheat isoamylase protein. It cannot be predicted by one of skill in the art that nucleic acids that hybridize to SEQ ID NO:1 or 3 under conditions as

specified above will encode a protein with the same activity as SEQ ID NO:2 and 4. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

The Applicants broadly claim any sequence that hybridizes with a nucleic acid of claim 24 or part thereof and then uses these sequences to transform host cells, plant cells, and plants for the purpose of over-expressing the polypeptide in the plant or in a system from which the protein will be recovered. But, based on the broad claim language, it is not certain that the claimed

nucleic acid will encode the desired protein especially since Applicant has not disclosed an assay for determining if an isolated nucleic acid encoding a polypeptide is a wheat isoamylase. Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe.

Altering the content or composition of starch by modulating the activity of an enzyme involved in the catabolism or metabolism of starch does not always lead to the expected result. Kossmann et al (1995, Carbohydrate Bioengineering, S.B. Petersen, B. Svensson and S Pedersen (Eds). Pages 271-278) teach that reducing the activity of granule bound starch synthase (GBSS) by antisense technology in potato did not effect the content or composition of starch, even though GBSS is involved in starch metabolism (page 275, paragraphs 4 and 5). Willmitzer et al (1993 In Plant Polymeric Carbohydrates; International Symposium Meuser, F., D.J. Manners and W. Seibel (Eds) Starch synthesis in transgenic plants, pages 33-39) teach transforming

potato with an antisense construct comprising the 35S CaMV promoter operably linked to the Branching Enzyme (BE) did not alter the total starch content or composition of starch in transgenic potato tubers (page 38, 4th paragraph).

Given the unpredictability of isolating a nucleic acid sequence with 65% or 90 % homology to SEQ ID NO:1 or a sequence that hybridizes to SEQ ID NO:1 and still maintains the same function as SEQ ID NO:2 for the reasons stated above; given the unpredictability of altering starch content or composition using an enzyme involved in starch catabolism or metabolism for the reasons stated above; given the lack of guidance and working examples for isolating a nucleic acid that exhibits 65% or 90% homology to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1 and maintains the function of SEQ ID NO:2, given the lack of working examples and guidance in determining if an isolated molecule is in fact a wheat isoamylase; and given the lack of guidance and examples of using an enzyme with 65% or 90% homology to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1 and maintains the function of SEQ ID NO:2 to alter the composition or content of starch in a plant; it would require undue experimentation by one skilled in the art to make and/or use the broadly claimed invention.

Claim Rejections - 35 USC § 102

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

6. Claims 24-28, 31-32, 35-42, 45, and 47-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Kossmann et al (July 1997, U.S. Patent 6,130,367).

The claims are broadly drawn to an isolated nucleic acid molecule encoding a protein with the function of a wheat isoamylase selected from the group consisting of: a nucleic acid molecule of SEQ ID NO:1 or part thereof , a nucleic acid molecule which hybridizes to any of the before-mentioned sequences, and a degenerate nucleic acid molecule of one of the before-mentioned sequences. Applicants also claim a nucleic acid molecule that hybridizes with a before-mentioned sequence and exhibits 65% or 90% homology to SEQ ID NO:1, including a vector, host cell, process for preparing a protein, transgenic plant cell and plant, all of which comprise a before-mentioned sequence operably linked to regulatory elements which ensure transcription.

Kossmann et al teach nucleic acid molecules that would hybridize with Applicants claimed invention given the broad claim language recited in claims 24 and 47. Kossmann et al also teach a vector, wherein said nucleic acid molecule is in sense orientation operably linked to elements that ensure transcription in eukaryotic and prokaryotic cells, a host cell, a plant cell and plant wherein the plant is a starch-storing plant all of which comprise the vector and said nucleic acid molecule. Kossmann et al also claim a method for producing a protein comprising said nucleic acid. Given Applicants broadly written claim language which includes molecules that hybridize to SEQ ID NO:1 and nucleic acid molecules whose nucleotide sequence deviates from that listed in SEQ ID NO:1 owing to the degeneracy of the genetic code, both of which would inherently encode molecules that are at least 65% of SEQ ID NO:1 and as such Kossmann et al anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 24-28, 31-32, 35-45, and 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kossmann et al (July 1997, U.S. Patent 6,130,367) taken with Vasil et al (April 1995, U.S. Patent 5,405,765).

The claims are drawn to an isolated nucleic acid molecule encoding a protein with the function of a wheat isoamylase selected from the group consisting of: a nucleic acid molecule of SEQ ID NO:1 or part thereof , a nucleic acid molecule which hybridizes to any of the before-mentioned sequences, and a degenerate nucleic acid molecule of one of the before-mentioned sequences. Applicants also claim a nucleic acid molecule that hybridizes with a before-mentioned sequence and exhibits 65% or 90% homology to SEQ ID NO:1, including a vector, host cell, process for preparing a protein, transgenic plant cell and plant, all of which comprise a before-mentioned sequence operably linked to regulatory elements which ensure transcription. Wherein the plant is a monocotyledous plant, in particular a barley, rye or wheat plant.

Kossmann et al teach a nucleic acid molecules that would hybridize with Applicants claimed invention given the broad claim language recited in claims 24 and 47. Kossmann et al also teach a vector, wherein said nucleic acid molecule is in sense orientation operably linked to elements that ensure transcription in eukaryotic and prokaryotic cells, a host cell, a plant cell and

plant wherein the plant is a starch-storing plant all of which comprise the vector and said nucleic acid molecule. Kossmann et al teach that the transformed plant could be of any desired species, and preferably in useful plants such as the monocots including wheat (column 8, lines 23-33). Kossmann et al also claim a method for producing a protein comprising said nucleic acid. Given Applicants broadly written claim language which includes molecules that hybridize to SEQ ID NO:1 and nucleic acid molecules whose nucleotide sequence deviates from that listed in SEQ ID NO:1 owing to the degeneracy of the genetic code, both of which would inherently encode molecules that are at least 65% of SEQ ID NO:1.

Kossmann et al do not specifically teach transforming a monocotyledonous plant wherein the monocot is a wheat plant

Vasil et al teach a method for transforming a wheat plant, which is categorized as a monocotyledonous plants.

Given the recognition of those of ordinary skill in the art of the value of transforming a plant with an enzyme involved in starch synthesis so as to engineer starch with a particular chemical structure and particularly in useful plants, such as wheat, as taught by Kossmann et al, it would have been obvious to use the method of Kossmann et al for the transformation of wheat plants, as taught by Vasil et al.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

8. Claims 24-28, 31-32, 35-42, 45-46, and 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kossmann et al (July 1997, U.S. Patent 6,130,367) taken with Baltensperger et al (April 1996, U.S. Patent RE. 35,202).

The claims are drawn to an isolated nucleic acid molecule encoding a protein with the function of a wheat isoamylase selected from the group consisting of: a nucleic acid molecule of SEQ ID NO:1 or part thereof , a nucleic acid molecule which hybridizes to any of the before-mentioned sequences, and a degenerate nucleic acid molecule of one of the before-mentioned sequences. Applicants also claim a nucleic acid molecule that hybridizes with a before-mentioned sequence and exhibits 65% or 90% homology to SEQ ID NO:1, including a vector, host cell, process for preparing a protein, transgenic plant cell and plant, all of which comprise a before-mentioned sequence operably linked to regulatory elements which ensure transcription. The Applicants also claim a process for the production of starch comprising isolating starch from plant material as claimed in claim 46.

Kossmann et al teach a nucleic acid molecules that would hybridize with Applicants claimed invention given the broad claim language recited in claims 24 and 47. Kossmann et al also teach a vector, wherein said nucleic acid molecule is in sense orientation operably linked to elements that ensure transcription in eukaryotic and prokaryotic cells, a host cell, a plant cell and plant wherein the plant is a starch-storing plant all of which comprise the vector and said nucleic acid molecule. Kossmann et al also claim a method for producing a protein comprising said nucleic acid. Given Applicants broadly written claim language which includes molecules that hybridize to SEQ ID NO:1 and nucleic acid molecules whose nucleotide sequence deviates from that listed in SEQ ID NO:1 owing to the degeneracy of the genetic code, both of which would

inherently encode molecules that are at least 65% of SEQ ID NO:1. In addition, Kossmann et al teach extracted starch and starch products (columns 9-13).

Kossmann et al do not teach a process for the production of starch.

Baltensperger et al teach a method of isolating starch from grain crops.

Given the recognition of those of ordinary skill in the art of the value of transforming a plant with an enzyme involved in starch synthesis so as to engineer starch with a particular chemical structure as taught by Kossmann et al for the production of starch and starch products, it would have been obvious to use the method of Kossmann et al and to isolate the starch from plant material as taught by Baltensperger et al.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Sonya Williams, whose telephone number is (703) 305-2272.

Stuart Baum Ph.D.

October 19, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800